REMARKS

Applicant respectfully requests entry of the amendments and remarks submitted herein. Claims 1 and 16-19 are amended, claims 20 and 21 are canceled, and claims 22 and 23 are added. Claims 1-19 and 22-23 are currently pending.

I. Claims Examined on the Merits

The Examiner has withdrawn claim 19 from further consideration, alleging that that claim is drawn to a non-elected invention/species. However, in the Restriction Requirement mailed February 23, 2006, claim 19 was included in the invention of Group I, which Group was elected in the Response to the Restriction Requirement submitted on March 16, 2006. Thus, Applicant respectfully submits that claim 19 should not be withdrawn from consideration and should be examined on its merits.

II. The Specification

The Examiner requested that the status of parent priority application be updated in the first line of the specification. Applicant has updated the specification as requested.

The Examiner objected to the abstract of the invention, alleging that it does not clearly describe the invention. Applicant has amended the abstract of the invention as requested.

III. The Rejections of the Claims under 35 U.S.C. 112, Second Paragraph

The Examiner rejected claims 1-18 under 35 U.S.C. 112, second paragraph, alleging that those claims are indefinite. As these rejections may be maintained with respect to the pending claims, they are respectfully traversed.

(a) The Examiner alleges that the phrase "effective to hybridize protein" in claim 1 is indefinite and suggests use of the phrase "effective to bind protein". Claim 1 has been amended as suggested by the Examiner.

(b) The Examiner alleges that the term "survivin-specific ligand" in claim 1 is indefinite. Claim 1 has been amended to recite a "Survivin-specific antibody".

(c) The Examiner alleges that the term "pro-apoptosis factor (PAF)-specific ligand" in claim 1 is indefinite. Claim 1 has been amended to recite a "pro-apoptosis factor (PAF)-specific antibody".

(d) The Examiner indicates that the term "the PAF" in claims 4-6 renders those claims vague and indefinite. In particular, the Examiner requested clarification if the term "the PAF" refers to a PAF-specific ligand or to the PAF itself. As described in the application as filed, e.g., at page 2, lines 29-31, Fas, BID, p53, DR4, DR5, TNF-R, and Caspase 8 are pro-apoptosis factors (PAFs), not PAF-specific ligands.

(e) The Examiner indicated that the phrase "the physiological sample" did not have adequate antecedent basis in claims 7 and 14. Claim 1 has been amended to provide antecedent basis for this term.

(f) The Examiner indicated that the phrase "the agent" did not have adequate antecedent basis in claim 16. This term has been removed from claim 16.

In view of the above, Applicant requests that the rejections of claims 1-18 under 35 U.S.C. 112, second paragraph, be withdrawn.

IV. The Rejection of the Claims under 35 U.S.C. 112, First Paragraph (Written Description)

The Examiner rejected claims 1-18 under 35 U.S.C. 112, first paragraph as failing to comply with the written description requirement. As this rejection may be maintained with respect to the pending claims, it is respectfully traversed.

Applicant asserts that the specification as originally filed provides an adequate written description of the claimed invention. Applicant may show adequate written description by demonstrating that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics that provide evidence that Applicant was in possession of the claimed invention, *i.e.*, complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics. *Enzo Biochem. v. Gen-Probe Inc.*, 323 F.3d 956, 963, 63 U.S.P.Q.2d 1609, 1613 (Fed. Cir. 2002). What is conventional or well known to one of ordinary skill in the art need not be disclosed in detail. *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.3d 1367, 1384, 231 U.S.P.Q. 81, 94 (Fed. Cir. 1986). Furthermore, the written description requirement states that the Applicant must describe the invention; it does not state that every

invention must be described in the same way. As each field evolves, the balance also evolves between what is known and what is added by each inventive contribution. *Capon v. Eshhar v. Dudas*, 2005 U.S. App. LEXIS 16865 (Fed. Cir. 2005). Moreover, it is not necessary that every permutation within a generally operable invention be effective in order to obtain a generic claim, provided that the effect is sufficiently demonstrated to characterize a generic invention. *Capon v. Eshhar v. Dudas*, 2005 U.S. App. LEXIS 16865 (Fed. Cir. 2005).

Independent claim 1 recites a diagnostic method for predicting the recurrence of a tumor or cancer in a human comprising:

> (a) contacting a human physiological sample suspected of being tumorigenic or cancerous with a Survivin-specific antibody that binds to mature human Survivin, wherein the Survivin-specific antibody comprises a first label, and a pro-apoptosis factor (PAF)-specific antibody comprising a second label under conditions effective to bind protein present in the tissue sample to the antibodies so as to yield a first population of protein bound to the Survivin-specific antibody and a second population of protein bound to the PAF-specific antibody;
> (b) quantifying the first and second populations of labeled protein to determine an amount of Survivin and an amount of PAF present in the sample; and
> (c) calculating the ratio of the amount of Survivin and the amount of PAF; wherein a Survivin:PAF ratio of more than about 1.5 is predictive that the tumor will recur.

The Examiner alleges that the specification does not provide adequate written description for a "Survivin-specific ligand". As amended, the claim 1 recites a "Survivin-specific antibody". Claim 1 is also amended to recite that the Survivin-specific antibody binds to mature human Survivin.

Thus, the claims recite identifying structural and functional characteristics of the Survivin-specific antibody, which antibody binds to mature human Survivin. Applicant thus respectfully asserts that sufficient detail of the identifying structural and functional characteristics of the claimed invention have been provided or were available to one of ordinary skill in the art at the time the application was filed, and as such, Applicant was in possession of the full scope of the claimed invention at the time the application was filed.

V. The Rejection of the Claims under 35 U.S.C. 112, First Paragraph (Enablement)

The Examiner rejected claims 1-18 under 35 U.S.C. 112, first paragraph, alleging that the specification does not reasonably provide enablement for a diagnostic method for predicting the recurrence of a tumor or cancer in any mammal by calculating the protein ratio of Survivin to PAF proteins wherein the ratio more than about 1.5 is predictive that the tumor will recur. As this rejection may be maintained with respect to the pending claims, it is respectfully traversed.

The Examiner alleges that the claims encompass tumor recurrence where the subject is any mammal. As amended, claim 1 recites a diagnostic method for predicting the recurrence of a tumor or cancer in a human.

The Examiner also alleges that expression of mRNA, specific for a tissue type, does not necessarily correlate nor predict equivalent levels of polypeptide expression. The Examiner acknowledges that the specification enables a diagnostic method for predicting the recurrence of a tumor or cancer in a human by quantifying the amount of Survivin protein. Further, Takamizawa *et al.* (*Journal of Pediatric Surgery*, *35*, 390-395 (2000), of record) present evidence that differences in the mRNA expression of the pro-apoptosis factor Fas translate into differences in actual Fas protein expression, which expression is correlated to kidney tumors. (*see*, *e.g.*, page 393 and the second full paragraph of column 2 on page 394)

Thus, Applicants respectfully submit that the claims satisfy the enablement requirement of 35 U.S.C. §112, first paragraph.

VI. The Rejection of the Claims under 35 U.S.C. 103(a)

Claims 1-18 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Lu *et al.* (*Cancer Research*, *58*, 1808-1812 (1998)) in view of LaCasse *et al.* (*Oncogene*, *17*, 3247-3259, (1998)), Adida *et al.* (*Lancet*, *351*, 882-883 (1998)), and Tamm *et al.* (*Cancer Research*, *58*, 5315-5320 (1998)). As this rejection may be maintained with respect to the pending claims, it is respectfully traversed.

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success

must both be found in the prior art and not based on Applicant's disclosure. MPEP Section 706.02(j).

Lu *et al.* disclose that Survivin correlated with tumor cell apoptosis and p53 accumulation in gastric carcinomas. Lu *et al.*, however, do not teach or suggest quantifying the amount of Survivin and the amount of PAF present in the sample. Further Lu *et al.* did not calculate the ratio of the amount of Survivin and the amount of PAF. Moreover, Lu *et al.* did not determine that a Survivin:PAF ratio of more than about 1.5 is predictive that the tumor will recur.

LaCasse *et al.* do not remedy the deficiencies of Lu *et al.* LaCasse *et al.* is a review article that discusses inhibitors of apoptosis (IAP), including Survivin. LaCasse *et al.*, however, do not teach or suggest quantifying the amount of Survivin and the amount of PAF present in the sample. Further LaCasse *et al.* did not calculate the ratio of the amount of Survivin and the amount of PAF. Moreover, LaCasse *et al.* did not determine that a Survivin:PAF ratio of more than about 1.5 is predictive that the tumor will recur.

Adida *et al.* do not remedy the deficiencies of Lu *et al.* and LaCasse *et al.* Adida *et al.* discuss the expression of Survivin in neuroblastoma and its relation to disease progression (p. 882). Adida *et al.*, however, do not teach or suggest quantifying the amount of Survivin and the amount of PAF present in the sample. Further Adida *et al.* did not calculate the ratio of the amount of Survivin and the amount of PAF. Moreover, Adida *et al.* did not determine that a Survivin:PAF ratio of more than about 1.5 is predictive that the tumor will recur.

Tamm *et al.* do not remedy the deficiencies of Lu *et al.*, LaCasse *et al.*, and Adida *et al.* Tamm *et al.* discuss the anti-apoptotic mechanism of surviving and its expression on 60 human tumor cell lines. Tamm *et al.* quantified the amount of survivin protein in human tumor cell lines (p. 5316). Tamm *et al.* studied the mechanistic interaction of Survivin on Fas in tumor cell lines. Tamm *et al.*, however, do not teach or suggest quantifying the amount of PAF present in a sample. Further Tamm *et al.* did not calculate the ratio of the amount of Survivin and the amount of PAF. Moreover, Tamm *et al.* did not determine that a Survivin:PAF ratio of more than about 1.5 is predictive that the tumor will recur.

Thus, the cited documents, even when combined, do not teach or suggest all the features of the claims. Therefore, the claims are not obvious over Lu *et al.*, LaCasse *et al.*, Adida *et al.* and Tamm *et al.*, and Applicant requests that this rejection be withdrawn.

CONCLUSION

Applicant respectfully submits that the claims are in condition for allowance, and notification to that effect is earnestly requested. The Examiner is invited to telephone Applicant's attorney at (952) 876-4091 to facilitate prosecution of this application.

If necessary, please apply any charges or credits to Deposit Account No. 50-3503.

Respectfully submitted,
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Date: 24 October 2006

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